Abstract Submitted
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Model systems to investigate the effect of cholesterol on the transfection efficiency of lipoplexes ALEXANDRA ZIDOVSKA, HEATHER M. EVANS, KAI EWERT, CYRUS R. SAFINYA, Materials, Physics, and Molecular, Cellular and Developmental Biology Departments, Santa Barbara, CA 93106 — Motivated by its important role in lipid-mediated gene delivery, we have studied the effect of cholesterol on membrane fusion. While recent work in our group has identified the membrane charge density as a critical parameter for transfection efficiency (TE) of lamellar, DOPC containing cationic lipid-DNA (CL-DNA) complexes [1-3], this model cannot fully explain the effect of cholesterol, suggesting that a different mechanism is responsible for the observed enhancement of TE. A model system using negatively charged giant vesicles has been developed to mimic the interaction of the cell membrane with CL-DNA complexes containing cholesterol. Differences in fusogenic properties have been observed as a function of the amount of cholesterol present in the CL-DNA complexes, and a fluorescence resonance energy transfer based assay was employed to quantify this effect. X-ray diffraction confirms that the lamellar structure seen with CL- DNA complexes is retained with the addition of cholesterol. Funding provided by NIH GM-59288 and NSF DMR-0503347. [1] A.J. Lin et al, *Biophys. J.*, 2003, V84:3307-3316. [2] K. Ewert et al, *J. Med. Chem.*, 2002, V45:5023-5029. [3] A. Ahmad et al., *J. Gene Med.,* 2005, V7:739-748.

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